Watershed Strokes After Cardiac Surgery
Diagnosis, Etiology, and Outcome

Rebecca F. Gottesman, MD; Paul M. Sherman, MD; Maura A. Grega, RN, MSN; David M. Yousem, MD, MBA; Louis M. Borowicz, Jr, MS; Ola A. Selnes, PhD; William A. Baumgartner, MD; Guy M. McKhann, MD

Background and Purpose—Watershed strokes are more prevalent after cardiac surgery than in other stroke populations, but their mechanism in this setting is not understood. We investigated the role of intraoperative blood pressure in the development of watershed strokes and used MRI to evaluate diagnosis and outcomes associated with this stroke subtype.

Methods—From 1998 to 2003 we studied 98 patients with clinical stroke after cardiac surgery who underwent MRI with diffusion-weighted imaging. We used logistic regression to explore the relationship between mean arterial pressure and watershed infarcts, between watershed infarcts and outcome, and $\chi^2$ analyses to compare detection by MRI versus CT of watershed infarcts.

Results—Bilateral watershed infarcts were present on 48% of MRIs and 22% of CTs ($P<0.0001$). Perioperative stroke patients with bilateral watershed infarcts, compared with those with other infarct patterns, were 17.3 times more likely to die, 12.5 and 6.2 times more likely to be discharged to a skilled nursing facility and to acute rehabilitation, respectively, than to be discharged home ($P=0.0004$). Patients with a decrease in mean arterial pressure of at least 10 mm Hg (intraoperative compared with preoperative) were 4.1 times more likely to have bilateral watershed infarcts than other infarct patterns.

Conclusions—Bilateral watershed infarcts after cardiac surgery are most reliably detected by diffusion-weighted imaging MRI and are associated with poor short-term outcome, compared with other infarct types. The mechanism may include an intraoperative drop in blood pressure from a patient’s baseline. These findings have implications for future clinical practice and research. (Stroke. 2006;37:2306-2311.)

Key Words: brain hypoxia-ischemia ■ cardiovascular surgical procedures ■ coronary artery bypass ■ outcomes assessment ■ stroke

Strokes occur in 3% to 9% of patients after cardiac surgery.1 Patients with postoperative strokes have up to a 10-fold increase in mortality2,3 and a 3-fold increase in hospital stay. In prior studies of stroke after cardiac surgery, stroke was mainly a clinical diagnosis. With postoperative computerized tomography (CT) and MRI, however, the location, distribution, and size of postoperative infarcts can be evaluated. These characteristics can then be associated with outcomes and possible mechanisms.

Watershed-distribution strokes are seen more frequently in patients with postcardiac surgery stroke than in the general stroke population (over 40% versus 2% to 5%, respectively).4-6 Patients with watershed infarcts by CT are more likely to require long-term care than other postcardiac surgery stroke patients.7

The mechanism underlying postcardiac surgery watershed stroke probably involves a combination of hypoperfusion and embolization,8 but the role of hypoperfusion has not been well elucidated. Watershed strokes in the general population are usually secondary to global hypoperfusion, such as during cardiac arrest, or are attributable to stenosis of the carotid artery or other major vessels, leading to local hypoperfusion.9

In cardiac surgery patients, global systemic hypoperfusion, caused by severe intraoperative hypotension, is known to be associated with poor outcomes.10,11 The role of more subtle changes in blood pressure is not well established: however, one randomized trial showed improved neurological and cardiac outcome in patients with mean arterial pressure (MAP) maintained at 80 to 100 mm Hg (versus 50 to 60 mm Hg),12 whereas others have hypothesized that neurological injury only occurs when cerebral perfusion pressure is below 50 mm Hg, even with moderate carotid stenosis.13

In the present study, we evaluated 98 patients who had a stroke after cardiac surgery and had postoperative MRI with diffusion-weighted imaging (DWI). We hypothesized that DWI MRI is more sensitive than CT in the detection of acute watershed infarction after cardiac surgery, that bilateral watershed strokes (among infarct types) are associated with poor

Received May 12, 2006; final revision received June 8, 2006; accepted June 28, 2006.
From the Johns Hopkins Medical Institutions (R.F.G., M.A.G., D.M.Y., O.A.S., W.A.B.), Baltimore, Md; the Wilford Hall Medical Center (P.M.S.), San Antonio, Tex; and the Johns Hopkins University (L.M.B., G.M.M.), Baltimore, Md.
Correspondence to Dr Guy M. McKhann, 338 Krieger Hall, Johns Hopkins University, 3400 N. Charles Street, Baltimore, MD 21218. E-mail guy.mckhann@jhu.edu
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Stroke is available at http://www.strokeaha.org

DOI: 10.1161/01.STR.0000236024.68020.3a
short-term outcome, and that changes in intraoperative blood pressure contribute to the development of watershed infarcts.

**Materials and Methods**

**Patients**

The local Institutional Review Board office approved this study. Since 1992, all patients undergoing cardiac surgery at Johns Hopkins Hospital in Baltimore, Md, were followed for development of new neurological deficits. In patients with a postoperative focal neurological deficit, neurological consultations were requested, and those with a clinical diagnosis of stroke were entered into the Cardiac Surgery Stroke Database. In this study, only those patients in this database from 1998 through 2003 who had an MRI with DWI were included. We defined intraoperative blood pressure as blood pressure while on cardiopulmonary bypass (CPB), so patients who underwent off-pump coronary artery bypass grafting (CABG) were excluded from the part of the study involving blood pressure measurements. In addition, for that part of the study, we excluded patients with symptom onset beyond 10 days postoperatively.

**Data Collection/Independent Variables**

The Cardiac Surgery Stroke database included the following prospectively collected data: demographic information, medical history including preoperative blood pressure, intraoperative physiological characteristics, in-hospital complications and discharge status. Change in MAP (equal to the average of MAPs recorded by the perfusionist every 15 minutes during CPB, subtracted from preoperative MAP) was calculated for inter-rater reliability. Pearson statistics were calculated to determine degree of inter-rater reliability; for MRI and CT combined, the $\kappa$ for all binary ratings was 0.58, with 84.4% agreement, and was 0.60 for nonbinary ratings. The $\kappa$ for bilateral watershed infarcts was 0.68.

**Neuroimaging Review**

Two reviewers (R.F.G. and P.M.S.), blinded to patient clinical information, retrospectively and independently reviewed all CTs and MRIs in their chronological order. Films were rated for the following stroke characteristics: infarct location and type (watershed, vertebrobasilar, territorial, lacunar), laterality, and size. Size of each stroke was rated by each reviewer, with 3 points for large infarct patterns (eg, $>2/3$ of middle cerebral artery territory), 2 for medium (1/3 to 2/3 of middle cerebral artery territory), and 1 for small (<1/3 of middle cerebral artery territory). A total volume score (for each patient and for each stroke type) was obtained by averaging the scores for each side and then summing the 2 sides. Patients could have multiple infarct types. After rating forms were completed, a third researcher (M.G.) identified areas of disagreement. Consensus was required for stroke type but not size classifications; if there was initial disagreement between the 2 reviewers, they subsequently met to make a consensus decision.

**Short-Term Outcome**

Discharge status (in-hospital death, discharge to nursing home/subacute rehabilitation, discharge to acute rehabilitation, and discharge to home) and length of stay were recorded at the time of discharge.

**Statistical Analysis**

Stata 8.0 for Macintosh was used for all analyses. $^1$ $^4$ $\kappa$ statistics were calculated for inter-rater reliability. Pearson $\chi^2$. Fisher exact tests and $t$ tests explored univariate relationships between variables of interest and imaging characteristics and determined difference in detection of watershed infarction by CT versus MRI.

Multinomial logistic regression models were used to determine the role of bilateral watershed infarcts in prediction of short-term outcome, and Fisher exact test was used to assess differences in length of stay between patients with bilateral watershed infarcts and those with other patterns. For regression models, we adjusted for potential confounding variables.

Logistic regression examined the role of blood pressure on radiographic findings (ie, presence of bilateral watershed infarcts). The relationships among various blood pressure indices (intraoperative mean MAP, lowest intraoperative MAP, and change in MAP) and development of bilateral watershed infarcts were each explored as continuous and as dichotomous variables. Ordinal logistic regression was used to determine the effect of blood pressure on watershed stroke volume. $P$ values were determined using likelihood ratio testing.

Interaction between carotid disease (assessed by duplex preoperatively) and blood pressure variation was also examined.

**Results**

A total of 98 patients were included in the study: 98 MRI films and 109 CT scans were reviewed (0 to 3 CTs per patient). All patients were included in the analyses of short-term outcome and in the comparison of CT to DWI MRI. For the analysis of the relationship between intraoperative blood pressure and watershed stroke, we excluded 5 patients with off-pump CABG and 2 patients with over 10 days between surgery and symptom onset, leaving 91 patients. Patients with bilateral watershed infarcts are compared with those with other infarct patterns in Table 1.

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**Diagnosis of Watershed Stroke**

Bilateral watershed infarcts were identified in 48% of MRIs (on DWI) and in 22% of CTs ($\chi^2=15.07, P<0.001$). Unilateral watershed infarcts were seen in 68% of DWI MRIs but only in 37% of brain CTs ($\chi^2=20.73, P<0.001$).

**Watershed Strokes and Short-Term Outcome**

Patients with bilateral watershed infarcts were compared with those with other infarct patterns (Table 1). Patients with bilateral watershed infarcts were more likely to have undergone an aortic procedure and less likely to have undergone a simple or redo CABG ($P=0.04$); they also had longer CPB times ($P=0.02$). Figure 1 shows 2 patients, 1 with a territorial infarct, and 1 with bilateral watershed strokes.

Patients who had bilateral watershed infarcts were 6.23 times as likely to be discharged to an acute rehabilitation facility, 12.46 times more likely to be discharged to subacute rehabilitation or to a skilled nursing facility, and 17.28 times more likely to die in the hospital than be discharged to home ($P=0.0004$; Table 2). A similar effect persisted even among patients with small to medium bilateral watershed infarcts: unadjusted odds ratios (ORs) for the same comparisons were 4.6 (95% CI: 1.2, 17.3), 6.8 (95% CI: 1.6, 28.2), and 11.2 (95% CI: 1.4, 89.6), respectively ($P=0.02$; not adjusted for bilateral old strokes attributable to limited sample size). Of 10 deaths in this population, 8 occurred in patients with bilateral watershed strokes (Figure 2).

Patients with a length-of-stay $>14$ days (median) were more likely to have bilateral watershed infarcts than other stroke patterns ($\chi^2=4.12, P=0.047$). Other major radiographic findings that differed between the 2 groups were examined as potential confounders, but did not change the point estimate for the relationship between bilateral watershed strokes and outcome. No other imaging findings were predictors of outcome after adjustment for watershed infarction.
Blood Pressure and Watershed Strokes

We performed univariate and multivariate logistic regression to explore the association between blood pressure and watershed stroke (Table 3). Patients with a drop in MAP of at least 10 mm Hg were 4.06 times (adjusted OR: 1.03, 15.98) as likely to develop bilateral watershed strokes as those patients who had a smaller drop or no drop in blood pressure. There was no significant continuous effect, with either a linear model or a nonlinear spline model. The model fit the data well (Hosmer-Lemeshow statistic, $P$=0.45). CPB time had an almost significant ($P$=0.055) effect in the multivariate model on development of bilateral watershed strokes (adjusted OR=1.09 per 10-minute increase in CPB time (95% CI: 0.99, 1.19)), with similar univariate results.

Among patients who had on-pump CABG surgery, the estimate was less precise (crude OR 3.7 [95% CI: 0.9, 15.0],

![Figure 1. Two MRI (DWI) images of 2 patients with postoperative infarcts: on the left, the patient had an acute territorial infarct, and the scan on the right demonstrates acute bilateral watershed strokes.](image-url)
adjusted OR 3.7 [95% CI: 0.6, 20.7]) for a larger compared with smaller drop in MAP.

There was a nonstatistically significant suggestion that patients with an increase in blood pressure from their preoperative baseline were also slightly more likely to have bilateral watershed strokes, although there were very few patients in this category.

When mean intraoperative MAP itself was split at the median (70 mm Hg), there was no effect (adjusted OR 1.3, \( P = 0.5 \)) for patients below the median (compared with those above it). Analysis of the lowest MAP during surgery, split at the median (60 mm Hg), revealed no significant relationship with bilateral watershed strokes (adjusted OR 1.4, \( P = 0.5 \)).

Size of watershed infarction was also examined as an outcome variable. When drop in MAP was dichotomized at a threshold of 10 mm Hg, as above, the adjusted odds of having a larger watershed total volume (compared with a smaller volume) was 3.2 (95% CI: 1.1, 9.5; \( P = 0.03 \) [adjusted for preoperative MAP, history of hypertension, presence of intraoperative circulatory arrest, and CPB time]).

### Carotid Disease and Blood Pressure

Preoperative carotid duplex results were available for 84 of the patients on whom analysis relating to carotid disease and change in blood pressure was performed. No significant interaction was found between change in blood pressure and presence of bilateral carotid disease (defined as >60% stenosis on each side) in development of bilateral watershed infarcts, although the sample size was too small to comment on whether this means an interaction is or is not truly present.

### Discussion

Our data show that bilateral watershed strokes are most readily detected by DWI MRI, are associated with poor short-term outcome among patients with a clinical diagnosis of stroke after cardiac surgery, and may be related to a decrease in intraoperative blood pressure from a preoperative baseline.

### Diagnosis of Watershed Strokes

Both unilateral and bilateral watershed strokes were seen more frequently on DWI MRI than on CT. Cardiac surgeons may be reluctant to obtain MRIs postoperatively given the required duration of the procedure, patients’ critical illness, and issues such as pacing wires. Our data demonstrate the advantage of obtaining MRIs, not only in prognostication, but because further information about specific stroke pattern can point to the need for appropriate interventions. DWI, in particular, is relatively quick to obtain and is uniquely sensitive to acute infarction. Moreover, the success of future research in areas such as neuroprotection and changes in surgical techniques will depend critically on obtaining accurate estimates of postop-

### Figure 2

Short-term outcome in postcardiac surgery stroke patients with and without bilateral watershed infarcts.

<table>
<thead>
<tr>
<th>Discharge Status</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge to acute rehabilitation</td>
<td>5.25 (1.50, 18.38)</td>
<td>6.23 (1.70, 22.79)</td>
</tr>
<tr>
<td>Discharge to skilled nursing facility</td>
<td>9.33 (2.43, 35.84)</td>
<td>12.46 (2.98, 52.13)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>21.00 (3.20, 137.98)</td>
<td>17.28 (2.48, 120.32)</td>
</tr>
</tbody>
</table>

*Adjusted for age, bilateral old infarcts (MRI), and acute territorial infarct.
erative infarction rates. Thus, better understanding of the mechanisms of postoperative stroke requires an accurate diagnosis.

**Short-Term Outcome After Watershed Strokes**

Most general stroke patients with watershed strokes have favorable outcomes. In the postcardiac surgery stroke population, however, it appears that having bilateral watershed strokes strongly predicts poor outcome, with 8 of the 10 deaths in this group occurring in patients with bilateral watershed infarcts. Nonsurgical patients with watershed strokes usually have unilateral infarcts and often have had gradual arterial stenosis, leading to formation of collaterals or to ischemic preconditioning. In contrast, many of the postoperative patients in our study had bilateral watershed infarcts and had more acute changes in cerebral perfusion. Our overall mortality rates (10.2%) are comparable with previous reports at our center and elsewhere.

**Blood Pressure and Watershed Strokes**

Evidence for a role of hypoperfusion during cardiac surgery has thus far been lacking, but our data suggest that a decrease in blood pressure from a preoperative baseline may increase the likelihood of watershed strokes. Although a strong relationship between MAP change and watershed stroke was not found, our data do suggest that the most important factor is change in blood pressure, not the absolute intraoperative MAP. These data also suggest that prolonged CPB may be a risk factor for the development of bilateral watershed strokes, in particular, perhaps because of increased opportunity for hypoperfusion during longer CPB.

Because cerebral autoregulatory curves vary among individuals, a person with baseline hypertension will have a shifted curve, and the lower limit below which cerebral blood flow is no longer adequately regulated is raised. If future studies confirm a role of intraoperative drop in blood pressure, appropriate management of blood pressure during surgery potentially could decrease the likelihood of developing watershed strokes and ultimately improve outcome. However, it is premature at this point to influence clinical management; a well-designed prospective study is needed to replicate these results and show the optimal range for blood pressure, the importance of duration of the blood pressure change, and any associated complications.

**Limitations**

Use of a clinical diagnosis of stroke as an inclusion criterion is a potential limitation of our results. Although most patients in our study had a neurological examination after surgery, preoperative examinations (clinical or radiographic) were not standard. This could lead to a biased sample of patients with stroke. If patients not included in this database had radiographic findings of bilateral watershed infarcts, for example, but were not clinically diagnosed with stroke (ie, in encephalopathic patients) and also had better outcomes, the association with poor outcome might appear stronger than it truly is. If these results are interpreted in the context of the patient population, however, they are still informative; among patients given a clinical diagnosis of stroke after cardiac surgery, there does appear to be an increased risk of poor short-term outcome in those patients with bilateral watershed strokes.

The periodicity of the blood pressure values may also limit interpretation. Although blood pressure is measured continuously during surgery, values are only recorded every 15 minutes which may underestimate both extremes of blood pressure values. Therefore, the mean MAP may not represent the true intraoperative blood pressure, and the lowest MAP recorded may not actually be the lowest pressure. Our data are also limited regarding duration of hypotension; the product of the level of hypotension and the duration of that hypotension may determine risk of cerebral hypoperfusion and watershed infarction. It is also likely that a relationship exists between carotid or intracranial disease and blood pressure; the sample size makes it difficult to draw conclusions regarding carotid disease. Future research is needed to address these concerns and further assess the role of variations in blood pressure during surgery on the development of stroke in general, as well as different stroke subtypes.

Understanding the impact of watershed strokes after cardiac surgery is important both for practical reasons (patient and family guidance, prognosis, and rehabilitation management), and because future research may benefit if the true burden of these and other strokes after cardiac surgery is well understood. Research in this population may also allow for better understanding of the etiology of watershed strokes in general, particularly regarding the relationship between embolization and hypoperfusion. Clinical use of DWI MRI will allow for better estimates of stroke rates after cardiac surgery, allowing for improved study design. In addition, future trials...
to improve surgical technique or trials of neuroprotective agents in cardiac surgery patients may be limited if other factors that affect outcome (such as stroke distribution) are not taken into account.

Summary
Bilateral watershed strokes are associated with poorer outcomes among patients with stroke after cardiac surgery. Identification of stroke characteristics that are associated with poor outcome may not only aid in prognostication in patients with strokes after cardiac surgery, but can identify areas for future intervention as more is understood about the mechanism of these strokes. Given their devastating consequences, we believe that future research should focus on prevention of watershed strokes, and future clinical evaluation should attend to the appropriate diagnosis of these strokes.

Acknowledgments
We appreciate Pamela Talalay’s editorial assistance.

Sources of Funding
This research was supported by National Institutes of Health grants K12(RG) and RO1-NS035610(GM) and the Dana Foundation.

Disclosures
None.

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Stroke. 2006;37:2306-2311; originally published online July 20, 2006;
doi: 10.1161/01.STR.0000236024.68020.3a
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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